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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/816,079	03/13/97	NIRONEN J	98-101

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EXAMINER	
BERMAN, A	
ART UNIT	**PAPER NUMBER**
1615	13

DATE MAILED: 05/23/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Offic Action Summary	Application No. 08/816,079	Applicant(s) WIRONEN ET AL.	
	Examiner Alysia Berman	Art Unit 1615	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statem nt(s) (PTO-1449) Paper No(s) _____ .
18)☒ Int rview Summary (PTO-413) Paper No(s). *14* .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

1. This office action obviates the previous final rejection, paper number 13, mailed 28 February 2000. Claims 1-37 are pending. The status of the claims is as follows:

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 6-13, 24, 28, 30 and 34-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Regarding claims 6-13 and 24, there is an open-ended bracket at line 1 of claim 6 that renders the claims indefinite. It is unclear what was deleted from the claim and, therefore, one cannot determine the metes and bounds of the claims.

5. Claims 8 and 9 recite the limitation "total **composite** weight" in line 2 of each claim. There is insufficient antecedent basis for this limitation in the claim. Claims 8 and 9 ultimately depend from claim 1, which recites a composition, not a composite.

6. Regarding claim 12, the deletion of "proteins" renders the claim indefinite. It is now unclear what the bone morphogenetic material is. It is suggested that "protein" be added to the claim.

7. Regarding claim 30, the phrase "other joints" renders the claim indefinite. It is unclear which joints are encompassed by this phrase. Therefore, the scope of the claims cannot be determined.

8. Regarding claims 28, 36 and 37, the phrase "U-shaped" renders the claims indefinite. The precise definition of U-shaped cannot be determined from the claims or the specification. Therefore, the metes and bounds of the claims cannot be determined.

9. Regarding claims 34-37, there are open-ended brackets in lines 1 and 2 of claim 34 that render the claims indefinite. It is unclear what was deleted from the claim and, therefore, one cannot determine the metes and bounds of the claims.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The instant application is directed to a composition comprising gelatin. The composition further comprises

A. antibiotics, bone morphogenetic protein, wetting agents, glycerol, carboxymethylcellulose, growth factors, steroids, NSAIDs or combinations thereof (claim 12),

B. at least 0.0001 mg/ml of bone growth factor (claim 22).

The composition is injection molded, vacuum molded, rotation molded, blow molded or extruded into a solid form (claim 27). The solid form is selected from vertebral disks, acetabular hemispheres, tubes, ellipsoid, oblong, or "U" shaped (claim 28). Claims 29, 30 and 32 are directed toward a method for inducing bone formation in vivo comprising implanting a composition comprising gelatin.

11. Claims 1-4 and 21 are rejected under 35 U.S.C. 102(a) as being anticipated by Ninomiya.

Ninomiya discloses heat-denatured bone matrix gelatin that is prepared by heat at 150°C for 30 minutes. Example 1 at page 15 of the instant specification and in claim 18, Applicant prepares the gelatin from demineralized bone matrix powder. The demineralized bone powder is treated with pepsin and then heated. Demineralized bone matrix would inherently contain osteogenic components such as bone morphogenetic protein. Although the demineralized bone matrix gelatin of the reference is heat-denatured, there is no teaching of removal of all osteogenic components. Therefore, Ninomiya appears to read on a composition comprising thermally treated gelatin and osteogenic components such as bone morphogenetic protein and other growth factors that was obtained in the same manner as Applicant.

12. Claims 1-6, 10-12, 21, 24, 27-30 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by US 4,191,747 (Scheicher '747).

US '747 discloses a corrective agent prepared by boiling gelatin in a physiological saline solution to dissolve and sterilize the gelatin (abstract). The gel-forming substance (gelatin) comprises about 0.5% to 30% by weight of the composition (col. 5, lines 29-33). The corrective agent preferably further contains an antibiotic (A) (col. 3, lines 4-5). Substances that stimulate bone formation or bone growth (B) may also be added to the corrective agent (col. 3, lines 45-

47). These substances include phosphorous, calcium (col. 3, lines 50-53), calcium phosphate hydroxyapatite crystals (col. 4, lines 1-7) and denatured bone meal (col. 4, lines 22-23). See also column 5, lines 48-58 for bone formation or bone growth stimulating substances in an amount from about 2.5-60% by weight (B).

The composition is prepared in disposable syringes and stored at room temperature above that at which the solution solidifies into a gel. It is also possible to cool the solution in the syringes and let it solidify into a gel (col. 6, lines 40-50). Before use, the composition is injected from the syringe into an ampoule at a temperature above that at which the solution solidifies into a gel (col. 7, lines 10-15). However, if the composition in the ampoule is not immediately used, it can be cooled and solidified until needed (col. 7, lines 43-45). Therefore, the prior art appears to read on the limitations of claim 27 of injection molding or extruding the composition and the solidified gel would be the shape of the ampoule, which is tubular or oblong (claim 28).

US '747 discloses at column 2, lines 10-42 that the composition is applied to wound surfaces, used as dental implants and used for open bone fractures, nailings and other bone operations. As stated above, the composition also comprises substances for stimulating bone formation or growth. The composition is used as an implant in bone fractures and other bone related wounds. Therefore, the induction of bone formation is inherent in the method of implanting the composition comprising bone formation stimulating substances.

The osteogenic components as recited in the claims are not considered a required limitation of the claims because they are recited based on a future intended use. Any properties exhibited by the components of the composition or the composition itself such as gelation temperature or molecular weight are inherent and are not given patentable weight over the prior

art composition. Therefore, US '747 discloses a composition comprising gelatin, antibiotics, and bone formation stimulating substances that is implanted into a dental cavity or a bone fracture site and would inherently induce bone formation.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1-6, 10-12, 21, 24, 27-30 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '747.

US '747 teaches all of the limitations of the claims as stated above. It does not explicitly teach a method for inducing bone formation *in vivo*.

Although it is the examiner's primary opinion that the implantation of the prior art composition would inherently induce bone formation, in the case that this may be argued, US '747 teaches that the composition is applied to wound surfaces, is useful as a dental implant and is useful in cases of open bone fractures, nailings and other bone operations as stated above. The composition comprises substances for stimulating bone formation and/or growth.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to implant the composition of US '747 *in vivo* with the reasonable expectation of inducing bone formation. The motivation to use the composition of US '747 to induce bone

formation flows logically from the art-recognized desire for implants that sterilely seal wounds and are reabsorbed after bone ingrowth.

15. Claims 7, 8, 13-20, 22, 23, and 33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '747 as applied to claims 1-6, 10-12, 21, 24, 27-30 and 32 above and further in view of US 5,422,340 (Ammann et al. '340).

US '747 teaches all of the limitations of the claims as stated in the 35 U.S.C. 102 and 103 rejections above. It does not teach deriving the gelatin or demineralized bone matrix from the species into which the bone paste is to be implanted (claims 7 and 8), between about 0.001 to 0.1 mg/ml of bone morphogenetic protein (claim 13), a frozen or freeze-dried composition (claim 14), from where the gelatin is obtained (claims 15-20), bone growth factor at a concentration of at least 0.001 mg/ml (claim 22), the bone growth factor is morphogenetic protein, TGF-beta, platelet derived growth factor (PDGF) or mixtures thereof (claim 23), the osteogenic components are demineralized bone matrix (DBM), bone morphogenetic protein, TGF-beta or mixtures thereof (claims 33 and 34).

US '340 discloses a formulation for inducing bone formation comprising TGF-beta and tricalcium phosphate. Lyophilized gelatin is disclosed at column 9, line 67. The derivation of components of the formulation from animals such as humans is disclosed at column 11, lines 17-33. The formulations are useful for treating periodontal disease, non-union fractures, spinal fusions, etc. (col. 12, lines 4-19). The formulation is implanted into the animal in the form of a molded implant, etc. (col. 12, lines 34-42). The TGF-beta is mixed with a biodegradable protein carrier such as gelatin to form a carrier matrix. The resultant mixture is dried and formed into an appropriate shape (col. 15, lines 49-54).

Claims 18-20 are not patentable over the prior art product because, although they recite a process by which the product is made, they are directed to the product. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method or production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

It is within the skill in the art to select optimal parameters in a composition in order to achieve a beneficial effect. *In re Boesch*, 205 USPQ 215 (CCPA 198). It is also considered within the skill in the art to shape the composition into any suitable form. Therefore, absent evidence of superior and unexpected results, these limitations are not considered critical to the invention.

It would have been obvious to one of ordinary skill in the art at the time of the invention to prepare the composition of US '747 and substitute the gelatin, bone growth factors and osteogenic components obtained from the animal source and shape the resultant composition into any appropriate shape as taught by US '340 in order to produce a implantable composition for inducing bone formation. The motivation lies in the art-recognized desire for an implantable bone formation inducing composition with enhanced consistency for improved application to the desired bone defect site.

16. Claims 13, 14, 22, 23, 25, 26 and 33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '747 as applied to claims 1-6, 10-12, 21, 24, 27-30 and 32 an further in view of US 5,484,601 ('601).

US '747 teaches all the limitations of the claims as stated in the 35 U.S.C. 102 and 103 rejections above. It does not teach 0.0001 to 0.1 mg/ml of bone morphogenetic protein (claim 13), a frozen solution or freeze-dried composition (claim 14), that the bone growth factor is morphogenetic protein, TGF-beta, PDGF, or mixtures thereof (claim 23), bone chips (claim 25), bone chips in the size range of 80 microns to 10 mm (claim 26), or osteogenic components selected from the group consisting of demineralized bone matrix (DBM), bone morphogenetic protein, TGF-beta, PDGF or mixtures thereof (claims 33 and 34).

US '601 teaches a bone powder composition for use in surgical bone repair (abstract). Bone chips obtained from cortical, cancellous and/or corticocancellous, allogeneic or xenogeneic bone tissue are disclosed at column 2, lines 3-17. The demineralized bone powder can be stored in a freeze-dried state (col. 2, lines 41-44). For bone morphogenetic proteins and TGF-beta, see column 3, lines 5-6. For gelatin used in the carrier, see column 3, line 63 to column 4, line 6. The example at column 4, lines 55-58 teaches the average particle size of the pulverized bone is about 100 to 300 microns. It is within the skill in the art to select optimal parameters in a composition in order to achieve a beneficial effect. *In re Boesch*, 205 USPQ 215 (CCPA 198). Therefore, the amount of bone morphogenetic protein is not considered critical to the invention, absent a showing of unexpected and superior results.

It would have been obvious to one of ordinary skill in the art at the time of the invention to prepare the composition of US '747 and substitute the bone chips, bone morphogenetic proteins and TGF-beta as taught by US '601 in order to produce a bone repair composition. The motivation stems from the art-recognized desire for a composition with a liquid or paste-like consistency that induces new bone ingrowth when applied to a bone defect site.

17. Claims 1-37 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over copending Application No. 09/014519 which has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e) if patented. This provisional rejection under 35 U.S.C. 103(a) is based upon a presumption of future patenting of the conflicting application.

The instant application is drawn to a composition comprising gelatin. Example 1 at pages 15 to 16 shows thermal treatment of the gelatin. Application 09/014159 is directed to a composition comprising thermally treated gelatin wherein the thermal treatment is sufficient to increase the kinematic viscosity of the gelatin. It would have been obvious to one of ordinary skill in the art to thermally treat the gelatin at an optimal temperature range in order to achieve a beneficial effect.

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective U.S. filing date of the copending application under 37 CFR 1.131.

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1-37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-44 of copending Application No. 09/014519. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the reasons stated in the provisional 35 U.S.C. rejection above.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

20. Claims 1-37 are directed to an invention not patentably distinct from claims 1-44 of commonly assigned Application number 09/014519. Specifically, for the reasons stated above.

Commonly assigned Application number 09/014159, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g).

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alysia Berman whose telephone number is 703/308-4638. The examiner can normally be reached on 8:00-4:30, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 703/308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703/305-3704 for regular communications and 703/305-3704 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-1234.

Alysia Berman
Patent Examiner
May 17, 2000

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